

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Rene Gantier et al.

Serial No. : 10/658,834

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Title : RATIONAL EVOLUTION OF CYTOKINES FOR HIGHER STABILITY,
THE CYTOKINES AND ENCODING NUCLEIC ACID MOLECULES

Art Unit : 1631

Examiner : Russell Scott Negin

Conf. No. : 7681

Appendix



Cytokine regions susceptible to protease attack identified by structural alignment with Lead mutants
of IFN α -2b

R

IFN- α 2b CDLPQTHSLGSRRTLMLLAQHRYfISLFSCLKDRHDFGFPQE~~EFGNQQFQKAETIPVLUHEMIOQQIFNL~~FSTKDSSAAWDETLIDKFYTYQQQLNDLEACVIQG
VGVETPLMKEDSILAVRKYTFQITLYLRRKKYSPCAEVRAEIMRSFSLSTNTI_QESLRSE

Exemplary protein of the interferons/interleukin-10 family

IFN- β MSYNLLGFLQRSSNFQCCQKLWQLNGRLIEYCLKDRMFIDPEEIKQLOQFQKEDAAALTIVEMQNIAPIPRQDSSSTGMNETIVENILLANYHQINHLKTVEEK
LEKEDEFTRGKLMSSLHLKRYXGRHLTYLKAREYSHCATIVREILLRNFYFINRLTGTYRN

Exemplary protein of the short-chain cytokines family

EPO APPRLICDSRVLERYLLEAKEAENITTCGAEHCSLINENITYPDTKVNFEYAWKRMKEVGOAVEVWQGLALLSEAVLRGQAALVVNSSSOPWEPOLHVDKAVSGLRSL
TTLRALGAQKEAISPPDAASAAAPLRTITAIDTFRKLFRVYSNFLRGKLLYTGEACRTGDR

Exemplary protein of the long-chain cytokines family

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 Application: René Gantier et al. Attorney/Deeckter No.: 17109-012001/922
 Encoding nucleic acid molecules for higher stability, the cytokines and
 rational evolution of cytokines for higher stability, the cytokines and
TPLGPASSLPQSFLLKCLEQVRKIQGDGAALQERLVSECATYKLCHPEELVLIGHSLUGPWAPLOSSCPSSQALQLAGCLSQLHSGLFLXQELIQALEGISPELGPPTLDLQL
DVADFATTIWQQMEELGMAPPALQPTQGAMPFAFASAFORAGGVVLVASHLQSFLEVSYRVLRHIAQP

FIG. 9

